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APPLICATION NO.	FILING DATE	FIRST NAMED INVENTOR	ATTORNEY DOCKET NO.	CONFIRMATION NO.
10/516,705	12/02/2004	Takahito Hara	3056 US0P	1003

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EXAMINER	
BRISTOL, LYNN ANNE	
ART UNIT	**PAPER NUMBER**
1643	

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05/15/2007	PAPER

Please find below and/or attached an Office communication concerning this application or proceeding.

The time period for reply, if any, is set in the attached communication.

Office Action Summary	Application No.	Applicant(s)	
	10/516,705	HARA ET AL.	
	Examiner	Art Unit	
	Lynn Bristol	1643	

-- The MAILING DATE of this communication appears on the cover sheet with the correspondence address --

Period for Reply

A SHORTENED STATUTORY PERIOD FOR REPLY IS SET TO EXPIRE 3 MONTH(S) OR THIRTY (30) DAYS, WHICHEVER IS LONGER, FROM THE MAILING DATE OF THIS COMMUNICATION.

- Extensions of time may be available under the provisions of 37 CFR 1.136(a). In no event, however, may a reply be timely filed after SIX (6) MONTHS from the mailing date of this communication.
- If NO period for reply is specified above, the maximum statutory period will apply and will expire SIX (6) MONTHS from the mailing date of this communication.
- Failure to reply within the set or extended period for reply will, by statute, cause the application to become ABANDONED (35 U.S.C. § 133). Any reply received by the Office later than three months after the mailing date of this communication, even if timely filed, may reduce any earned patent term adjustment. See 37 CFR 1.704(b).

Status

1)☐ Responsive to communication(s) filed on *09 March 2007*.

2a)☐ This action is **FINAL**. 2b)☒ This action is non-final.

3)☐ Since this application is in condition for allowance except for formal matters, prosecution as to the merits is closed in accordance with the practice under *Ex parte Quayle*, 1935 C.D. 11, 453 O.G. 213.

Disposition of Claims

4)☒ Claim(s) *1-70* is/are pending in the application.

4a) Of the above claim(s) *1-11 and 13-70* is/are withdrawn from consideration.

5)☐ Claim(s) _____ is/are allowed.

6)☒ Claim(s) *12* is/are rejected.

7)☐ Claim(s) _____ is/are objected to.

8)☐ Claim(s) _____ are subject to restriction and/or election requirement.

Application Papers

9)☒ The specification is objected to by the Examiner.

10)☐ The drawing(s) filed on _____ is/are: a)☐ accepted or b)☐ objected to by the Examiner.

Applicant may not request that any objection to the drawing(s) be held in abeyance. See 37 CFR 1.85(a).

Replacement drawing sheet(s) including the correction is required if the drawing(s) is objected to. See 37 CFR 1.121(d).

11)☐ The oath or declaration is objected to by the Examiner. Note the attached Office Action or form PTO-152.

Priority under 35 U.S.C. § 119

12)☐ Acknowledgment is made of a claim for foreign priority under 35 U.S.C. § 119(a)-(d) or (f).

a)☐ All b)☐ Some * c)☐ None of:

1.☐ Certified copies of the priority documents have been received.

2.☐ Certified copies of the priority documents have been received in Application No. _____.

3.☐ Copies of the certified copies of the priority documents have been received in this National Stage application from the International Bureau (PCT Rule 17.2(a)).

* See the attached detailed Office action for a list of the certified copies not received.

Attachment(s)

1) ☒ Notice of References Cited (PTO-892)
2) ☐ Notice of Draftsperson's Patent Drawing Review (PTO-948)
3) ☒ Information Disclosure Statement(s) (PTO/SB/08) Paper No(s)/Mail Date *12/2/04 and 9/18/06*.
4) ☐ Interview Summary (PTO-413) Paper No(s)/Mail Date. _____.
5) ☐ Notice of Informal Patent Application
6) ☐ Other: _____.

DETAILED ACTION

1. Claims 1-70 are all the pending claims in the application.

Election/Restrictions

2. Applicant's election with traverse of Group V (Claim 12) in the reply filed on 3/9/07 is acknowledged. The traversal is on the ground(s) that the claims recite a technical feature that is special and makes a contribution over the prior art (cited references).

Applicant's arguments are found persuasive with respect to the Veldscholte et al, Culig et al. and Furr et al. references discussed on pp. 1-2 of the Reply.

Applicant's arguments are not found persuasive with respect to the Hara et al. reference because Applicant's have not provided any showing of written support in the Japanese language patent application filed June 3, 2002 (JP 2002-162206) to substantiate their priority claim over the Hara publication date.

The requirement is still deemed proper and is therefore made FINAL.

3. Claims 1-11 and 13-70 are withdrawn from further consideration pursuant to 37 CFR 1.142(b), as being drawn to a nonelected inventions, there being no allowable generic or linking claim. Applicant timely traversed the restriction (election) requirement in the reply filed on 3/9/07.

4. Claim 12 is the pending claim under examination for this application.

Information Disclosure Statement

5. The U.S. and foreign patent references and the non-patent literature references cited in the IDS' of 12/2/04 and 9/18/06 have been considered and entered.

Specification

6. The specification is objected to for the following reasons:

a) The specification does not cross-reference the priority documents.

b) The use of trademarks e.g., polysorbate 80™ Triton X- 100™, have been noted in this application. A trademark should be capitalized wherever it appears and be accompanied by the generic terminology.

Although the use of trademarks is permissible in patent applications, the proprietary nature of the marks should be respected and every effort made to prevent their use in any manner which might adversely affect their validity as trademarks.

Applicants are advised to carefully check the entire specification for any other trademarks that are not properly identified.

Claim Rejections - 35 USC § 112

The following is a quotation of the second paragraph of 35 U.S.C. 112:

> The specification shall conclude with one or more claims particularly pointing out and distinctly claiming the subject matter which the applicant regards as his invention.

7. Claim 12 is rejected under 35 U.S.C. 112, second paragraph, as being indefinite for failing to particularly point out and distinctly claim the subject matter which applicant regards as the invention.

a) Claim 12 is indefinite because if the drug is to be selected on the basis of cancer cell susceptibility to the drug, then the cancer cell should not proliferate in long-term culture in the presence of the drug. The claim is constructed to recite that the culture is examined for the appearance of cells capable of proliferating, when instead it would seem that examining cultures for those cells that do not proliferate would result in the desired drug selection. Is induction of cancer resistance to a drug quantitatively and/or qualitatively the same as a cancer cell proliferating in the presence of the drug? Clarification is required.

b) Claim 12 is indefinite for the recitation "having...little potential to induce resistant cancer" because the phrase "little potential" is not defined by the claims or the specification. What degree of drug resistance is contemplated by the term "little". Is a "little potential" even measurable and what criteria define this?

c) Claim 12 recites the limitation "said conditions". There is insufficient antecedent basis for this limitation in the claim.

Claim Rejections - 35 USC § 102

The following is a quotation of the appropriate paragraphs of 35 U.S.C. 102 that form the basis for the rejections under this section made in this Office action:

> A person shall be entitled to a patent unless –
>
> (a) the invention was known or used by others in this country, or patented or described in a printed publication in this or a foreign country, before the invention thereof by the applicant for a patent.
> (b) the invention was patented or described in a printed publication in this or a foreign country or in public use or on sale in this country, more than one year prior to the date of application for patent in the United States.

8. Claim 12 is rejected under 35 U.S.C. 102(a) as being anticipated by Hara et al. (Cancer Research 63:149-153 (1/1/03); cited in the IDS of 9/18/06).

Claim 12 is drawn to a method of screening for antiandrogen drugs which produce little or no cancer resistance, where the method involves culturing an androgen-sensitive cancer cell in the presence of the drug and determining whether or not the cancer cells proliferate in the presence of the drug.

Hara teach screening the anti-androgen, bicalutamide, where an androgen-sensitive cancer cell is cultured in the presence of the drug under the selection conditions, and the drug is screened on the basis of establishing the long-term, proliferating cell line, LNCaP-FGC.

9. Claim 12 is rejected under 35 U.S.C. 102(b) as being anticipated by Long et al (Can. Res. 60:6630-6640 (2000)).

The interpretation of Claim 12 is discussed supra.

Long discloses screening antiandrogen compounds for their in vitro growth inhibitory effects on the androgen-dependent prostate cancer cell line, LNCaP. Long discloses using the cell line in culture to compare the efficacy of test compounds $C_{17,20}$-lyase, 5α-reductase, ketoconazole and finasteride with known inhibitor, flutamide, and measuring growth effects in vitro by culturing for 9 days (Figure 2A, Figure 3). Long observes differences over time in the appearance of the cell line ability to proliferate depending on the culture conditions.

10. Claim 12 is rejected under 35 U.S.C. 102(b) as being anticipated by Foury et al (J. Steroid Biochem. Molec. Biol. 66:235-240 (1998)).

The interpretation of Claim 12 is discussed supra.

Foury discloses comparing androgen responsive cell lines (LNCaP, R2 and MOP) *in vitro* for ability to proliferate in studies comparing two different antiandrogen drugs (CYPA and RU 56187). Foury discloses that R2 is inhibited by RU 56187 and MOP is inhibited by CYPA and RU 56187. Foury observes differences over time in the appearance of the different cell lines abilities to proliferate depending on the culture conditions.

Claim Rejections - 35 USC § 103

The following is a quotation of 35 U.S.C. 103(a) which forms the basis for all obviousness rejections set forth in this Office action:

> (a) A patent may not be obtained though the invention is not identically disclosed or described as set forth in section 102 of this title, if the differences between the subject matter sought to be patented and the prior art are such that the subject matter as a whole would have been obvious at the time the invention was made to a person having ordinary skill in the art to which said subject matter pertains. Patentability shall not be negatived by the manner in which the invention was made.

The factual inquiries set forth in *Graham* **v.** *John Deere Co.*, 383 U.S. 1, 148 USPQ 459 (1966), that are applied for establishing a background for determining obviousness under 35 U.S.C. 103(a) are summarized as follows:

1. Determining the scope and contents of the prior art.
2. Ascertaining the differences between the prior art and the claims at issue.
3. Resolving the level of ordinary skill in the pertinent art.
4. Considering objective evidence present in the application indicating obviousness or nonobviousness.

11. Claim 12 is rejected under 35 U.S.C. 103(a) as being unpatentable over Taplin et al. (Cancer Research, (1999), pp. 2511-2515, Vol. 59, No. 11; cited in the IDS of 12/2/04) in view of Joly-Pharaboz et al (J. Steroid Biochem. Molec. Biol. 55:67-76 (1995)).

The interpretation of Claim 12 is discussed supra.

At the time of Applicants invention, it would have been obvious to have used an *in vitro* antiandrogen drug selection process for identifying drugs that do not induce cancer resistance using a cancer cell line based on the combined disclosures of Taplin and Joly-Pharaboz.

Taplin discloses that AR mutations in tumor cells occur in response to strong selective pressure from flutamide (antiandrogen) treatment *in vivo* and that these mutations result in drug resistance for some patients and continued tumor cell survival and proliferation. Taplin discloses that other methods are needed to prevent a small number of tumor cells from surviving or escaping the initial inhibitory effects of AR antagonists such as targeting AR-associated coactivator proteins, downstream target genes, or signal transduction pathways that interact with AR which can be used alone or in combination with androgen blockade therapy. Taplin does not disclose an in vitro drug screening method which Joly-Pharaboz recitifies in its disclosure.

Joly-Pharaboz disclose drug selection for androgen-responsive cell lines *in vitro* under culture conditions with chronic treatment of androgens and antiandrogens, where cell proliferation under long-term culture is used to assess induction of drug resistance.

Joly-Pharaboz discloses the antiandrogen drugs, hydroxyflutaminde or cyproteropne acetate, as examples of drugs that induce cell proliferation in the screening method.

One skilled in the art would have been motivated to have produced the drug screening method and been reasonably assured of success at the invention was made based on the combined disclosure of Taplin and Joly-Pharaboz. The concept of selecting drugs that do not induce resistant cancer cell lines (with or without mutated ARs) was well understood within the field of art at the time of the invention. Taplin teaches induction of antiandrogen resistant cancer cells *in vivo* and the need to identify other methods that target tumor cells that escape the effects of antiandrogen drugs such as observed with flutamide, and Joly-Pharaboz disclose successful *in vitro* drug selection methods using drug-cultured cells from androgen-sensitive cancers where sensitivity to the drug is measured by inhibition of cell proliferation. One skilled in the art would have been assured of success in creating the instant claimed method because Taplin discloses the problems with administering a single antiandrogen drug over long-term treatment and the need to identify other inhibitors associated with AR or tumor targeting and Joly-Pharaboz already appreciated in vitro drug screening to select for antiandrogens that do not induce cancer resistance.

For all of these reasons, the claimed invention was prima facie obvious over Taplin and Joly-Pharaboz.

Conclusion

12. No claims are allowed.

13. References found to be relevant to Claim 12 are:

BENTEL, J., et al., In Vitro Cellular & Developmental Biology- Animal, (1999), Vol. 35, No. 10, pages 655-662 (cited in the IDS 9/18/06)

ZHAO, X., et al., The Journal of Urology, (1999), Vol. 162,pages 2192-2199 (cited in the IDS 9/18/06).

14. Any inquiry concerning this communication or earlier communications from the examiner should be directed to Lynn Bristol whose telephone number is 571-272-6883. The examiner can normally be reached on 8:00-4:00, Monday through Friday.

If attempts to reach the examiner by telephone are unsuccessful, the examiner's supervisor, Larry Helms can be reached on 571-272-0832. The fax phone number for the organization where this application or proceeding is assigned is 571-273-8300.

Information regarding the status of an application may be obtained from the Patent Application Information Retrieval (PAIR) system. Status information for published applications may be obtained from either Private PAIR or Public PAIR. Status information for unpublished applications is available through Private PAIR only. For more information about the PAIR system, see http://pair-direct.uspto.gov. Should you have questions on access to the Private PAIR system, contact the Electronic Business Center (EBC) at 866-217-9197 (toll-free). If you would like assistance from a USPTO Customer Service Representative or access to the automated information system, call 800-786-9199 (IN USA OR CANADA) or 571-272-1000.

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